

### AMENDMENTS TO THE DRAWINGS

The attached sheets of drawings show changes to Figures 3 and 4. For Figure 3, a clearer copy of the photograph is provided. For Figure 4A, "Figure 1." and the space between "of" and "barcode" have been deleted. After "start/end", "marke" has been replaced with --markers--, and where "markers" has been written in after "reading frame", it has been replaced with type written --markers--. For Figure 4B, "Figure 2." and the space between "of" and "barcode" have been deleted. For Figure 4C, "Figure 3." and the space between "of" and "barcode" have been deleted. These replacement sheets replace the original sheets filed with the application.

Attachment: Two (2) Replacement Sheets

Two (2) Annotated Sheet Showing Changes

## REMARKS

Applicants respectfully request entry of amendments to claims 1, 2, 6, 9-12, 14, 20, 21, and 29. Support for the amendments can be found throughout the specification, including paragraphs [0017], [0042], [0044], [0045], [0046], [0047], and the originally filed claims and, therefore, do not add new matter.

Applicants submit that pending claims 1-36 are in condition for allowance, and respectfully request that the claims as amended be entered.

## Objections

Applicants have corrected the specification at paragraph [0013], line 3, to provide the appropriate U.S. Ser. No. in the blank space that previously appeared. No new matter has been added. Applicants have corrected the specification at paragraphs [0183] and [0187] to remove hyperlinks from the specification, and have amended the specification to include the material previously incorporated by reference. Further, Applicants provide the following statement in accordance with 37 C.F.R. §1.57(f): the material being inserted is the material previously incorporated by reference and the amendment contains no new matter.

Claims 9 and 21 have been corrected in accordance with the suggestions offered in the Action.

Applicants have provided herewith corrected Figure 3, Figure 4A, Figure 4B, and Figure 4C.

For these reasons, Applicants respectfully request that the objections be withdrawn.

## Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 1-36 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite.

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

Claim 1 no longer recites “associated with” so the rejection is rendered moot. Applicants have amended the claim to recite “attached to.” The term would be understood by one of skill in the art. As such, one of skill in the art would understand the metes and bounds of the claim.

Regarding claims 1, 15, 16, 20, 24, 29, and 33, the Office Action alleges that the term “detectable non-encoding feature” is vague and indefinite because the instant application does not distinguish between a detectable non-encoding feature and an undetectable non-encoding feature. Applicants submit that there is no such requirement to meet the second paragraph standard.

Respectfully, in Exxon Research & Engineering Co. v. United States, 60 U.S.P.Q.2d 1272 (Fed. Cir. 2001) the court stated that “the standard for assessing whether a patent claim is sufficiently definite to satisfy the statutory requirement as follows: If one skilled in the art would understand the bounds of the claim when read in light of the specification, the claim satisfies section 112 second paragraph.” Further, as stated in Markman v. Westview Instruments, Inc., 34 U.S.P.Q.2d 1321 (Fed. Cir. 1995) (in banc), *aff’d* 38 U.S.P.Q.2d 1461 (1996), “As we have often stated, a patentee is free to be his own lexicographer . . . . The caveat is that any special definition given to a word must be clearly defined in the specification.”

Applicants have provided a specific definition for the term at issue at paragraph [0017]. As Applicants can be their own lexicographer when such a definition is provided, and as one of skill in the art would understand the bounds of the claims when read in light of the definition as recited, that is all that is required, and to require that a contrasting definition be provided is not supported by the case law or the M.P.E.P. Further, “non-encoding” cannot be separated from the phrase “detectable non-encoding feature” because its meaning as defined in the specification would be eviscerated if parsed in the manner suggested by the Action.

Regarding the recitation “coded probes,” while Applicants do not acquiesce to the reasoning offered in the Office Action, and to expedite prosecution toward allowance, claim 2 has been amended.

Regarding the recitation “substantially all possible sequences,” as stated for “detectable non-encoding feature,” Applicants have provided a specific definition for the term at issue at paragraph [0074]. However, while Applicants do not acquiesce to the reasoning offered in the

Office Action, and to expedite prosecution toward allowance, claim 2 has been amended to more clearly define the invention.

Regarding the recitation “the nucleic acid,” while Applicants do not acquiesce to the reasoning offered in the Office Action, and to expedite prosecution toward allowance, claims 6, 10, 11, and 12 have been amended.

Regarding the term “molecular combing,” the term is art recognized and is disclosed in the specification as such at paragraph [0066], including an explanation of the technique at paragraph [0087].

Regarding the term “are analyzed” while Applicants do not acquiesce to the reasoning offered in the Office Action, and to expedite prosecution toward allowance, claim 14 has been amended.

The term “associated with the nanocode,” in claim 15 clearly means that a molecular nanocode possesses encoded information regarding the probe to which it is attached and that such a probe can be identified by that encoded information (see, e.g., paragraph [0044]). Respectfully, “[i]f one skilled in the art would understand the bounds of the claim when read in light of the specification, the claim satisfies section 112 second paragraph” (see, e.g., Exxon Research & Engineering Co. v. United States, 60 U.S.P.Q.2d 1272 (Fed. Cir. 2001)). Therefore, as one of skill in the art would know the metes and bound of “associated with” when read in light of paragraph [0044] of the instant specification, the claim is not indefinite.

Regarding the recitation “check sum barcode segment,” the term is art recognized, the plain meaning of which is:

“Checksum-the sum of a group of data items, which sum is used for checking purposes (used in error detection and correcting).” (See, e.g., <http://www.its.bldrdoc.gov/fs-1037/dir-007/0950.htm>).

“Barcode” and “segment” are self explanatory. As such, one of skill in the art would know the metes and bound of the term, thus, the claim is not indefinite.

Regarding the recitation “single molecule level surface analysis method,” (of which scanning probe microscopy is a member) the term is art recognized, the plain meaning of which is:

Several related technologies for imaging and measuring surfaces on a fine scale, down to the level of molecules and groups of atoms, which share the concept of scanning an extremely sharp tip (3-50 nm radius of curvature) across an object surface. (See, e.g., <http://www.mobot.org/jwcross/spm/spm-introduction.htm>).

As such, one of skill in the art would know the metes and bounds of the term, thus, the claim is not indefinite.

For these reasons, Applicants respectfully request that the rejections be withdrawn.

**Rejections Under the Judicially Created Doctrine of Obviousness-Type Double Patenting**

Claims 20-28 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting allegedly over claims 1, 4, 5, 9-18, and 28-31 of co-pending U.S. Application Ser. No. 10/241,152.

Applicants submit that the Action is in error as a patent has been granted for U.S. Application Ser. No. 10/241,152 (i.e., cannot be provisionally rejected), further, the claims to the '152 application are directed to a method of making a sign (i.e., the subject matter of the patent is wholly independent and distinct).

For these reasons, Applicants respectfully request that the rejection against claims 20-28 be withdrawn.

Claims 1-15, 29-32, and 35 stand provisionally rejected under the judicially created doctrine of obviousness double patenting allegedly over claims 10-14 and 29-31 of co-pending U.S. Application Ser. No. 10/241,152.

Again, Applicants submit that the Action is in error as a patent has been granted for U.S. Application Ser. No. 10/241,152 (i.e., cannot be provisionally rejected), further, the claims to the '152 application are directed to a method of making a sign (i.e., the subject matter of the patent is wholly independent and distinct).

For these reasons, Applicants respectfully request that the rejection against claims 1-15, 29-32, and 35 be withdrawn.

Claims 20-32 and 35 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting allegedly over claims 1-28 of co-pending U.S. Application Ser. No. 10/667,004.

Applicants submit that the Action is in error regarding claims 1-25 of U.S. Application Ser. No. 10/667,004 because the subject matter of claims 20-32 and 35 of the present application are directed to compositions and systems, while claims 1-25 of the '004 application are directed to methods of targeting (i.e., claims are not for the same invention). As stated in Studiengesellschaft Kohle mbH v. Northern Petrochemical Co., 228 U.S.P.Q. 837 (CAFC 1986):

“Two patents that claim different classes of subject matter--a composition (a catalyst, issued 1963) and a process (polymerizing ethylene using that catalyst, issued 1978)—are not for the “same invention.”

Further, as there was no evidence offered as to the scope and content of the pertinent art, the level of skill in the art, or what would have been obvious to a person skilled in the art, the court held that under such facts (i.e., as are present here) there was no obviousness double patenting. Studiengesellschaft Kohle mbH, at 841.

Regarding claims 26-28 of the cited reference, the M.P.E.P. states at §804:

“Any obviousness-type double patenting rejection should make clear

- (A) The differences between the inventions defined by the conflicting claims – a claim in the patent compared to a claim in the application; and
- (B) The reasons why a person of ordinary skill in the art would conclude that the invention defined in the claim at issue would have been an obvious variation of the invention defined in a claim in the patent.”

Respectfully, the Action fails to meet either of these requirements, and thus, has failed to offer that any analysis was employed in the instant obviousness-type double patenting rejection that parallels the guidelines of a 35 U.S.C. §103 obviousness determination as required (See, e.g., In re Braat, 19 U.S.P.Q.2d 1289 (Fed. Cir. 1991) and M.P.E.P. §804(B)(1)).

As such, a conclusion of obviousness type double patenting cannot be made because 1) the standards as provided in Studiengesellschaft Kohle mbH v. Northern Petrochemical Co. have

not been met and 2) no evidence is offered supporting that a factual determination required for 103 was employed.

For these reasons, Applicants respectfully request that the rejection against claims 20-32 and 35 be withdrawn.

Claims 1-4, 9, and 12-14 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting allegedly over claims 10, 11, and 21 of co-pending U.S. Application Ser. No. 10/667,004.

Applicants submit that the Action has not met the requirement for rejection under the judicially created doctrine of obviousness-type double patenting.

The '004 application is silent with respect to a nanocode comprising a detectable non-encoding feature; i.e., the disclosure is deficient with respect to teaching this element. The M.P.E.P. states at §804(B)(1) that since the analysis employed in an obviousness-type double patenting determination parallels the guidelines for a 35 U.S.C. §103(a) rejection, the factual inquiries set forth in Graham v. John Deere Co., 148 U.S.P.Q. 459 (1966) are to be employed. As stated above, these factual inquiries are summarized as follows:

- “Any obviousness-type double patenting rejection should make clear
  - (A) The differences between the inventions defined by the conflicting claims – a claim in the patent compared to a claim in the application; and
  - (B) The reasons why a person of ordinary skill in the art would conclude that the invention defined in the claim at issue would have been an obvious variation of the invention defined in a claim in the patent.”

In view of the deficiency identified in the '004 application, there is no explanation of the differences between the claims or any reasoning offered to explain why the skilled artisan would be motivated to modify the claims of the '004 application to meet the elements of the instant claims. Therefore, the Action fails to meet either of above requirements, and thus, has failed to offer that any analysis was employed in the instant obviousness-type double patenting rejection that parallels the guidelines of a 35 U.S.C. §103 obviousness determination as required (See, e.g., In re Braat, 19 U.S.P.Q.2d 1289 (Fed. Cir. 1991) and M.P.E.P. §804(B)(1)).

For these reasons, Applicants respectfully request that the rejection against claims 1-4, 9, and 12-14 be withdrawn.

Claims 20-32 and 35 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting allegedly over claims 1-27 of co-pending U.S. Application Ser. No. 11/077,577.

Applicants submit that the Action has not met the requirement for rejection under the judicially created doctrine of obviousness-type double patenting.

The '577 application is silent with respect to a nanocode comprising a detectable non-encoding feature; i.e., the disclosure is deficient with respect to teaching this element. The M.P.E.P. states at §804(B)(1) that since the analysis employed in an obviousness-type double patenting determination parallels the guidelines for a 35 U.S.C. §103(a) rejection, the factual inquiries set forth in Graham v. John Deere Co., 148 U.S.P.Q. 459 (1966) are to be employed. As stated above, these factual inquiries are summarized as follows:

“Any obviousness-type double patenting rejection should make clear  
(A) The differences between the inventions defined by the conflicting claims – a claim in the patent compared to a claim in the application; and  
(B) The reasons why a person of ordinary skill in the art would conclude that the invention defined in the claim at issue would have been an obvious variation of the invention defined in a claim in the patent.”

In view of the deficiency identified in the '577 application, there is no explanation of the differences between the claims or any reasoning offered to explain why the skilled artisan would be motivated to modify the claims of the '577 application to meet the elements of the instant claims. Therefore, the Action fails to meet either of above requirements, and thus, has failed to offer that any analysis was employed in the instant obviousness-type double patenting rejection that parallels the guidelines of a 35 U.S.C. §103(a) obviousness determination as required (See, e.g., In re Braat, 19 U.S.P.Q.2d 1289 (Fed. Cir. 1991) and M.P.E.P. §804(B)(1)).

For these reasons, Applicants respectfully request that the rejection against claims 20-32 and 35 be withdrawn.

Claims 1-4, 9, and 12-14 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting allegedly over claims 10 and 11 of co-pending U.S. Application Ser. No. 11/077,577.

Applicants submit that the Action has not met the requirement for rejection under the judicially created doctrine of obviousness-type double patenting.

The '577 application is silent with respect to a nanocode comprising a detectable non-encoding feature; i.e., the disclosure is deficient with respect to teaching this element. The M.P.E.P. states at §804(b)(1) that since the analysis employed in an obviousness-type double patenting determination parallels the guidelines for a 35 U.S.C. §103(a) rejection, the factual inquiries set forth in Graham v. John Deere Co., 148 U.S.P.Q. 459 (1966) are to be employed. As stated above, these factual inquiries are summarized as follows:

- “Any obviousness-type double patenting rejection should make clear
  - (A) The differences between the inventions defined by the conflicting claims – a claim in the patent compared to a claim in the application; and
  - (B) The reasons why a person of ordinary skill in the art would conclude that the invention defined in the claim at issue would have been an obvious variation of the invention defined in a claim in the patent.”

In view of the deficiency identified in the '577 application, there is no explanation of the differences between the claims or any reasoning offered to explain why the skilled artisan would be motivated to modify the claims of the '577 application to meet the elements of the instant claims. Therefore, the Action fails to meet either of above requirements, and thus, has failed to offer that any analysis was employed in the instant obviousness-type double patenting rejection that parallels the guidelines of a 35 U.S.C. §103(a) obviousness determination as required (See, e.g., In re Braat, 19 U.S.P.Q.2d 1289 (Fed. Cir. 1991) and M.P.E.P. §804(B)(1)).

For this reason, Applicants respectfully request that the rejection against claims 1-4, 9, and 12-14 be withdrawn.

## Rejections Under 35 U.S.C. §102

Claims 1-36 stand rejected under 35 U.S.C. §102(e), as allegedly being anticipated by Chan et al. (U.S. Patent App. No.: 2004/0058328) or Chan et al (U.S. Patent App. No.: 2004/0126820).

Applicants traverse the rejection, as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

The Office Action alleges, in pertinent part, that the cited references, in the alternative, teach the elements as recited in the present claims. However, review of the cited references shows that neither teaches nor suggests detectable non-encoding features.

The present claims expressly recite “oligonucleotide probes comprising . . . a detectable non-encoding feature”.

As stated in Hybritech Inc. v. Monoclonal Antibody, Inc., 231 U.S.P.Q. 81 (Fed. Cir. 1986), “It is axiomatic that for prior art to anticipate under 102 it has to meet every element of the claimed invention.”

Therefore, because the instant claims recite an element that is not taught or suggested in either of the cited references, these cited references do not anticipate the claimed invention.

Failure of the prior art to meet every element of the claimed invention does not meet the standard under 102. For these reasons, Applicants respectfully request that the rejection be withdrawn.

Claims 20-24 and 28 stand rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Han et al.

Applicants traverse the rejection, as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

The Office Action alleges, in pertinent part, that the cited reference teaches the elements as recited in the present claims. However, review of the cited reference shows that neither coded oligonucleotides comprising detectable non-encoding features nor that such features serve as a quality control check for detecting nanocodes and/or distinguishes target nucleotides from self-assembled coded oligonucleotide probe structures are taught or suggested.

The present claims expressly recite these elements.

As stated in Hybritech Inc. v. Monoclonal Antibody, Inc., 231 U.S.P.Q. 81 (Fed. Cir. 1986), "It is axiomatic that for prior art to anticipate under 102 it has to meet every element of the claimed invention."

Therefore, because the instant claims recite elements that are not taught or suggested in the cited reference, the cited reference does not anticipate the claimed invention.

Failure of the prior art to meet every element of the claimed invention does not meet the standard under 102. For these reasons, Applicants respectfully request that the rejection be withdrawn.

#### Rejection Under 35 U.S.C. §103

Claims 1-4, 9-15, 20-23, 26, 28-32, and 35 stands rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Mirkin et al. in view of Nygren et al.

Applicants traverse the rejection, as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First there must be some suggestion or motivation in the references themselves or in knowledge generally available to one of skill in the art, to modify the reference or combine the reference teachings. Second, there must be a reasonable expectation of success. And, finally the prior art reference (or references when combined) must teach all claim limitations. The teaching or suggestion and reasonable expectation of success must both be found in the prior art and not in Applicants' disclosure. (See M.P.E.P. §706.02(j)).

Applicants submit that because the cited references do not teach all the claim limitations, one of skill in the art would not be motivated to combine the reference teachings.

The Office Action intimates, in pertinent part, that Mirkin et al. is silent with respect to using scanning microscopy to detect nucleic acids in nucleic acid molecular hybridization assay. The Action then provides Nygren et al. to cure the deficiency identified in the primary reference. However, review of Mirkin et al. demonstrates that the reference does not teach an oligonucleotide probe comprising detectable non-encoding features nor that such features serve as a quality control check for detecting nanocodes and/or distinguishes target nucleotides from

self-assembled coded oligonucleotide probe structures, elements presently recited in the claims. Neither are these elements taught or suggested in Nygren et al.

Because the teachings of Mirkin et al. would not result in a method (or composition or system) comprising the elements as claimed when combined with the teachings of Nygren et al., one of skill in the art would not have an expectation of success since the invention as claimed would not be achieved in view of such teachings. Therefore, one of skill in the art would not be motivated to combine such teachings.

Again, the “teaching or suggestion and reasonable expectation of success must **both** be found in the prior art.” (Emphasis added). One cannot simple use the Applicants’ disclosure as a “blueprint” to reconstruct, by hindsight, Applicants’ claim. See, e.g., Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 227 U.S.P.Q. 543 (Fed. Cir. 1985). Because there is neither the suggestion nor expectation of success that can be found in the cited art, no *prima facie* case of obviousness has been established.

Applicants submit that because there is no reasonable expectation of successfully achieving the invention as claimed, there is no motivation to combine the cited references, thus, no *prima facie* case for obviousness exists. For these reasons, Applicants respectfully request that the rejection, including as it might be applied against the amended claims, be withdrawn.

In the event that the Patent and Trademark Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. **070702007000**.

Dated: July 14, 2006

Respectfully submitted,

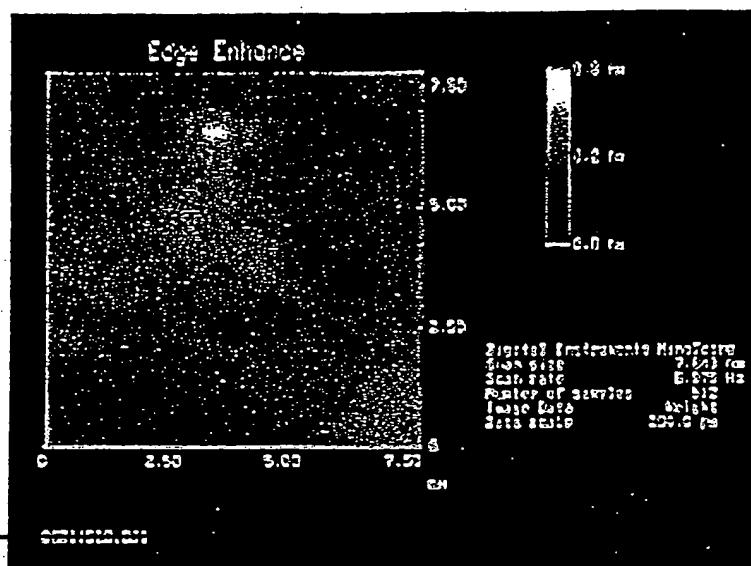
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Title: METHODS AND COMPOSITIONS FOR DETECTING  
NUCLEIC ACIDS USING SCANNING PROBE MICROSCOPY AND  
NANOCODES  
ANNOTATED SHEET



FIG. 3



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ANNOTATED SHEET

FIG. 4A

Figure 1. Example of barcode with molecular feature tags for reading frames and start/end markers.

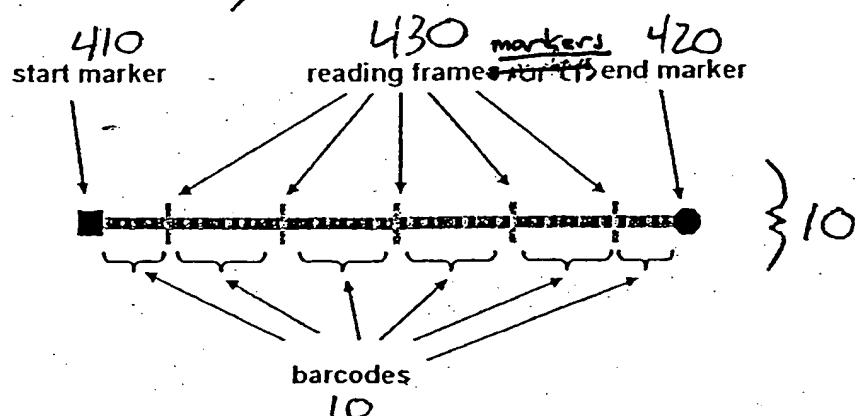


FIG. 4B

Figure 2. Example of barcode transformed into molecular feature tags for data compression.

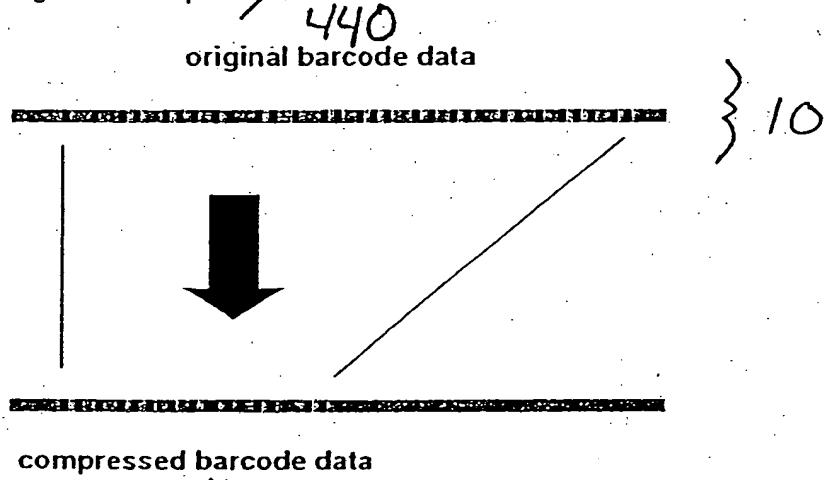


FIG. 4C

Figure 3. Example of barcode with molecular feature tags for check sum.

